Neural Encoding Models

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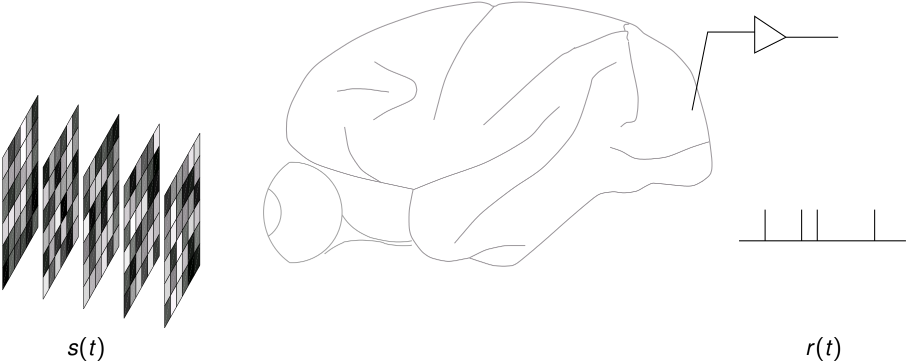
Computation plays a vital part in systematising empirical data.

Stimulus coding



Decoding: $\hat{s}(t) = G[r(t)]$ (reconstruction)

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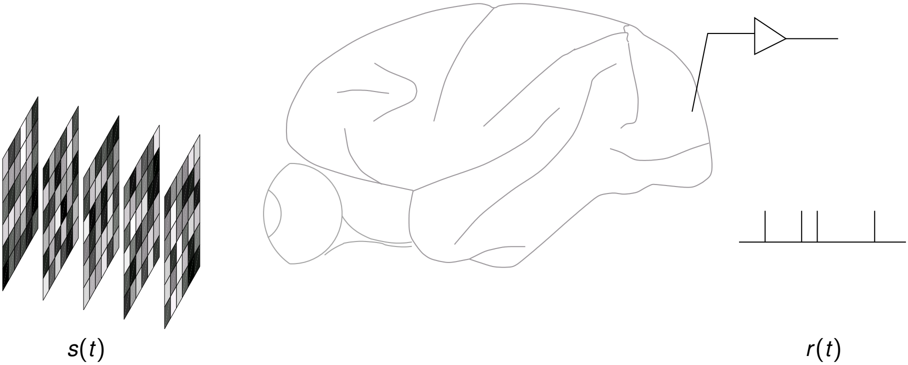

Decoding: $\hat{s}(t) = G[r(t)]$ (reconstruction)

Encoding: $\hat{r}(t) = F[s(t)]$ (systems identification)

Why?

The stimulus coding problem has sometimes been identified with the “neural coding” problem.

However, on the face of it, mapping *either* the decoding or encoding function does not by itself answer either of our basic questions about coding.

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- design hypothesis-driven stimulus-coding models: evaluate coding reliability for different function(al)s of $s(t)$ and for different definitions of $r(t)$.
- but correlation $\not\Rightarrow$ causation: in this case the *presence* of information about an aspect of the stimulus in a particular aspect of the response does not mean that the brain *uses* that information.

General approach

Goal: Estimate $p(\text{spike}|s, H)$ [or *intensity* $\lambda(t|s[0, t), H(t))$] from data.

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- Select stimuli efficiently
- Fit models with smaller numbers of parameters

Spikes, or rate?

Most neurons communicate using action potentials — statistically described by a point process:

$$P\big(\text{spike} \in [t, t + dt)\big) = \lambda(t|H(t), \text{stimulus}, \text{network activity})dt$$

To fully model the response we need to identify λ. In general this depends on spike history $H(t)$ and network activity. Three options:

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$$\overline{\lambda}(t, \text{stimulus}) = \lim_{N\to\infty} \frac{1}{N} \sum_n \lambda(t|H_n(t), \text{stimulus}, \text{network}_n)\,,$$

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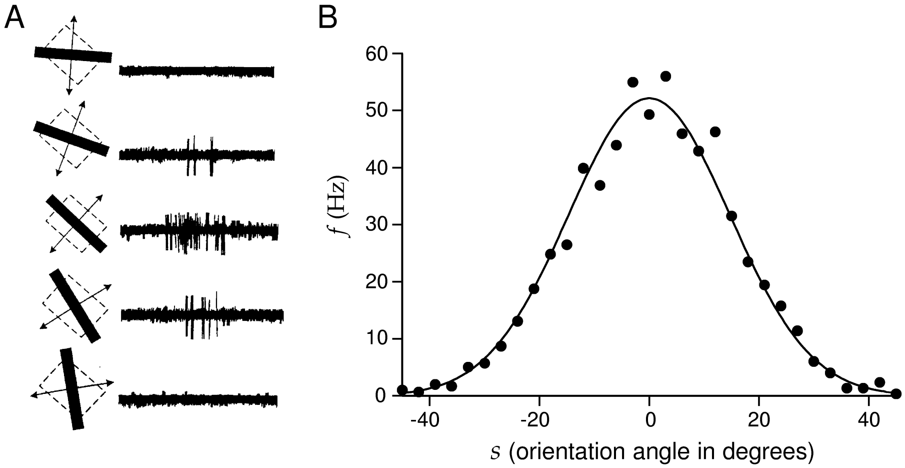
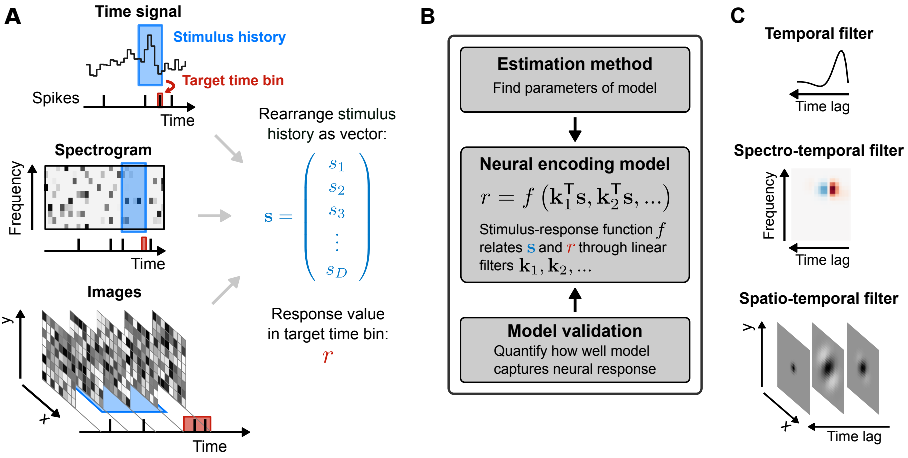
  and try to fit this.
- Attempt to capture history and network effects in simple models.

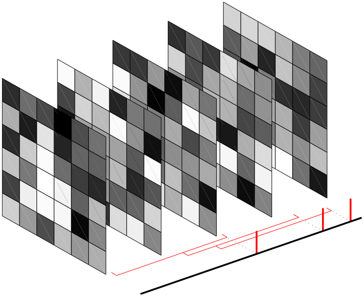
Tuning – stationary stimuli

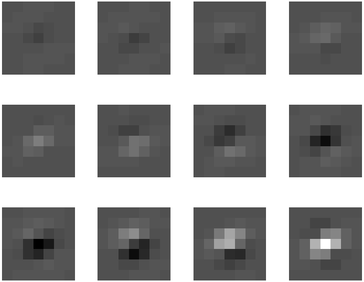


(Nonlinear) filtering – dynamic stimuli



Spike-triggered average





Decoding: mean of P $(s \mid r = 1)$

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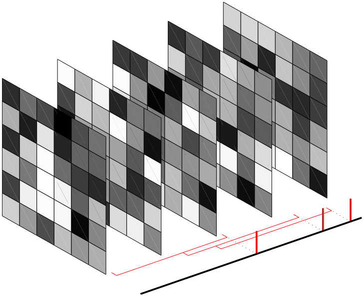

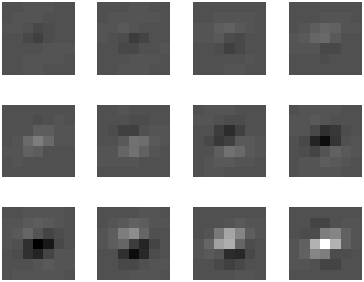

Decoding: mean of $\mathrm{P}\,(s \mid r = 1)$

Encoding: predictive filter

Linear regression

$$s_1 \quad s_2 \quad s_3 \quad \ldots \quad s_T \quad s_{T+1} \quad \ldots$$

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$$SW = R$$

$$W(\omega) = \frac{S(\omega)^* R(\omega)}{|S(\omega)|^2}$$

$$W = \underbrace{(S^{\mathsf{T}} S)}_{\Sigma_{SS}}{}^{-1} \underbrace{(S^{\mathsf{T}} R)}_{\text{STA}}$$

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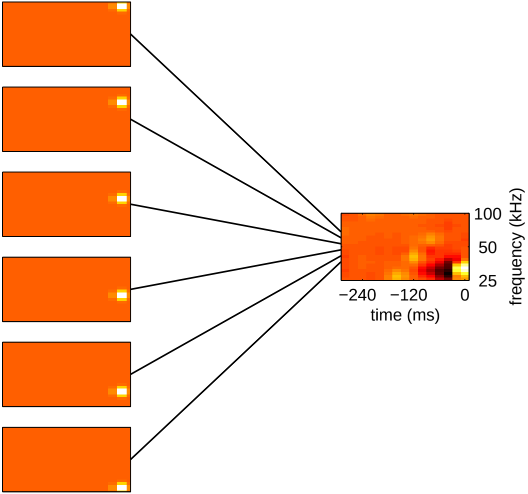
  - interpretable suggestions of underlying sensitivity (but see later)
  - may provide unbiased estimates of cascade filters (see later)

Likelihood penalties for regularisation

$$\widehat{\mathbf{w}} = \underset{\mathbf{w}}{\operatorname{argmax}} \underbrace{\mathcal{L}(\mathbf{w}; \mathit{Data})}_{\text{Likelihood}} \quad - \underbrace{\mathcal{R}(\mathbf{w})}_{\text{Regulariser}}$$

$\mathcal{R}$ may penalise large values of $\mathbf{w}$ (e.g. $\|\mathbf{w}\|^2$ or $\sum_i |w_i|$) or may promote smoothness or other properties.

Appropriate priors



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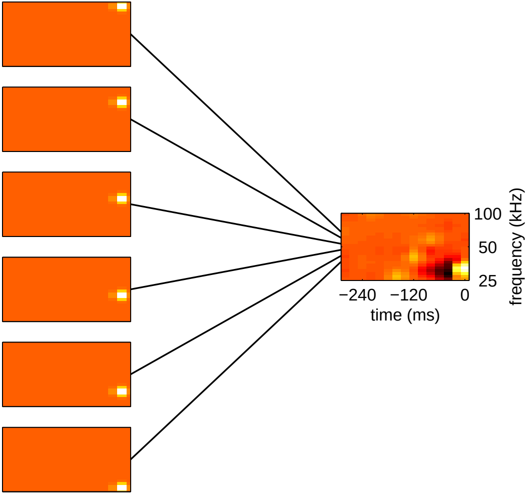

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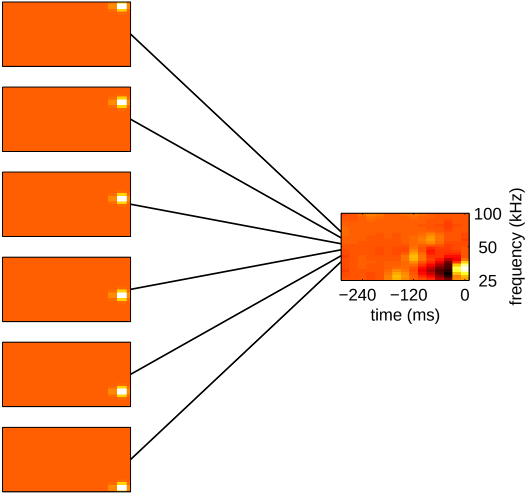

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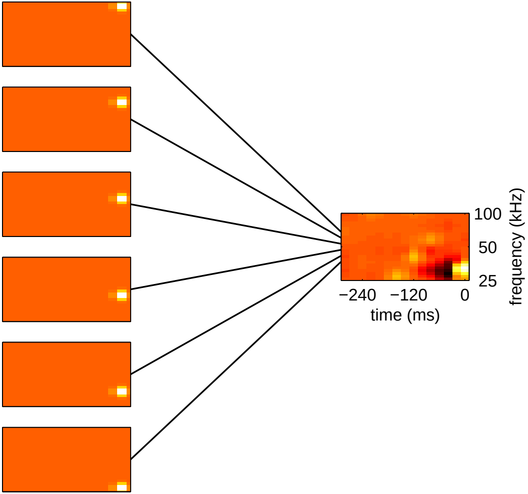
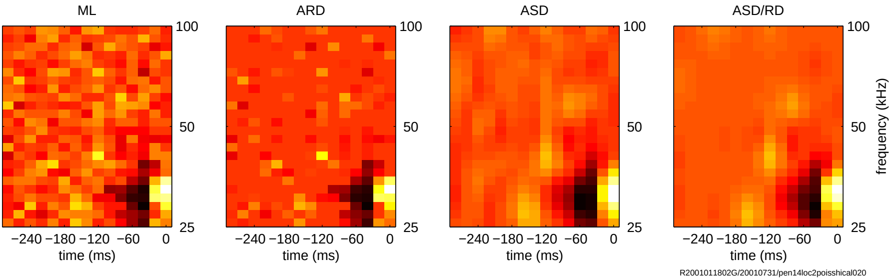
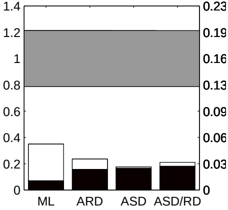


- sparsity [C_{ii} zero for many i] ARD
- smoothness [C_{ij} high for close i and j] ASD
- locality [C_{ii} high in a single region] ALD

Smoothness and sparsity (ASD/RD)





Beyond linearity

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Linear models often fail to predict well. Alternatives?

- Wiener/Volterra functional expansions
  - M-series
  - Linearised estimation
  - Kernel formulations
- LN (Wiener) cascades
  - Spike-trigger covariance (STC) methods
  - "Maximimally informative" dimensions (MID) $\Leftrightarrow$ ML nonparametric LNP models
  - ML Parametric GLM models
- NL (Hammerstein) cascades
  - Multilinear formulations
- LNLN and more . . .

The Volterra functional expansion

A polynomial-like expansion for functionals (or operators).

Let $y(t) = F[x(t)]$. Then:

$$y(t) \approx k^{(0)} + \int d\tau\, k^{(1)}(\tau)x(t-\tau) + \iint d\tau_1\, d\tau_2\, k^{(2)}(\tau_1, \tau_2)x(t-\tau_1)x(t-\tau_2)$$
$$+ \iiint d\tau_1\, d\tau_2\, d\tau_3\, k^{(3)}(\tau_1, \tau_2, \tau_3)x(t-\tau_1)x(t-\tau_2)x(t-\tau_3) + \ldots$$

or (in discretised time)

$$y_t = K^{(0)} + \sum_i K_i^{(1)} x_{t-i} + \sum_{ij} K_{ij}^{(2)} x_{t-i}x_{t-j} + \sum_{ijk} K_{ijk}^{(3)} x_{t-i}x_{t-j}x_{t-k} + \ldots$$

For finite expansion, the kernels $k^{(0)}, k^{(1)}(\cdot), k^{(2)}(\cdot,\cdot), k^{(3)}(\cdot,\cdot,\cdot), \ldots$ are not straightforwardly related to the functional F. Indeed, values of lower-order kernels change as the maximum order of the expansion is increased.

Estimation: model is linear in kernels, so can be estimated just like a linear (first-order) model with expanded “input”.

- Kernel trick: polynomial kernel $K(x_1, x_2) = (1 + x_1 x_2)^n$.
- M-series.

Wiener Expansion

The Wiener expansion gives functionals of different orders that are orthogonal *for white noise input* $x(t)$.

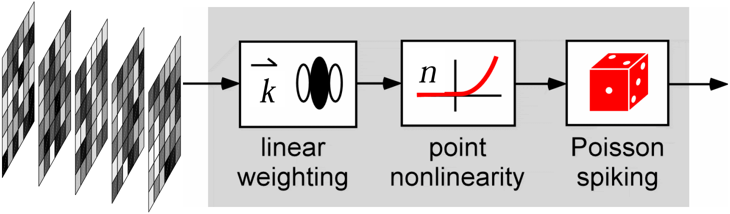
$$\begin{aligned}
G_0[x(t); h^{(0)}] &= h^{(0)} \\
G_1[x(t); h^{(1)}] &= \int d\tau\, h^{(1)}(\tau)x(t-\tau) \\
G_2[x(t); h^{(2)}] &= \iint d\tau_1\, d\tau_2\, h^{(2)}(\tau_1,\tau_2)x(t-\tau_1)x(t-\tau_2) - P\int d\tau_1\, h^{(2)}(\tau_1,\tau_1) \\
G_3[x(t); h^{(3)}] &= \iiint d\tau_1\, d\tau_2\, d\tau_3\, h^{(3)}(\tau_1,\tau_2,\tau_3)x(t-\tau_1)x(t-\tau_2)x(t-\tau_3) \\
&\qquad - 3P\iint d\tau_1\, d\tau_2\, h^{(3)}(\tau_1,\tau_2,\tau_2)x(t-\tau_1)
\end{aligned}$$

Easy to verify that $\mathbb{E}[G_i[x(t)]G_j[x(t)]] = 0$ for $i \neq j$.

Thus, these kernels can be estimated independently. But, they depend on the stimulus.

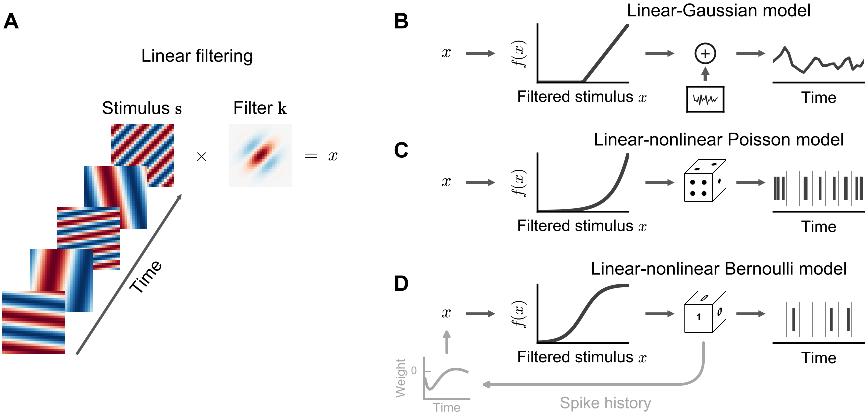
Cascade models

The LNP (Wiener) cascade

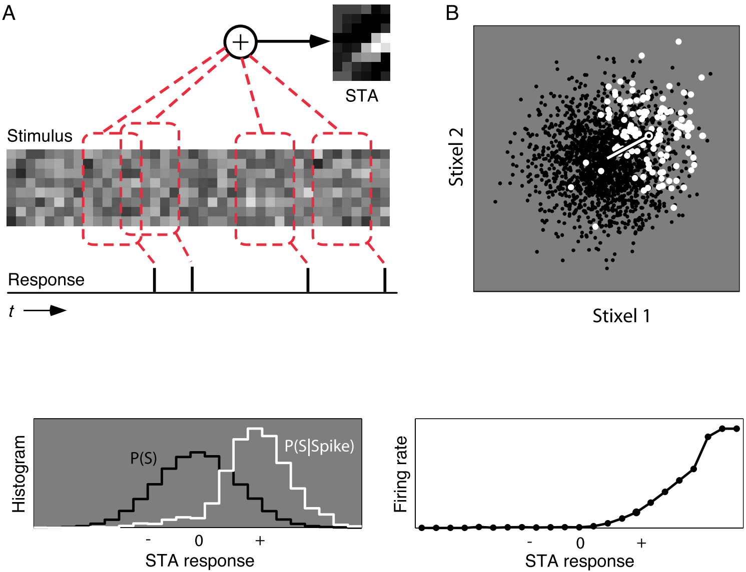


- Rectification addresses negative firing rates.
- Loose biophysical correspondance.

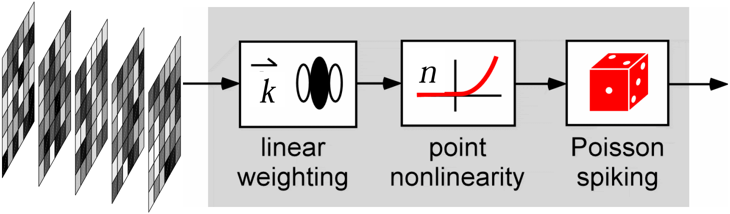
LNP cascades and noise



LNP estimation – the Spike-triggered ensemble

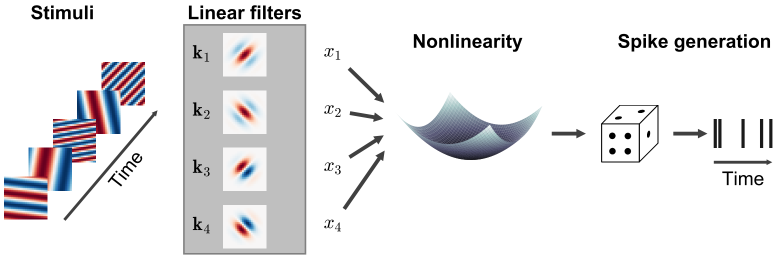


Single linear filter



- STA is unbiased estimate of filter for spherical input distribution. (Bussgang's theorem)
- Elliptically-distributed data can be whitened $\Rightarrow$ linear regression weights are unbiased.
- Linear weights are not necessarily maximum-likelihood (or otherwise optimal), even for spherical/elliptical stimulus distributions.
- Linear weights may be biased for general stimuli (binary/uniform or natural).

Multiple filters

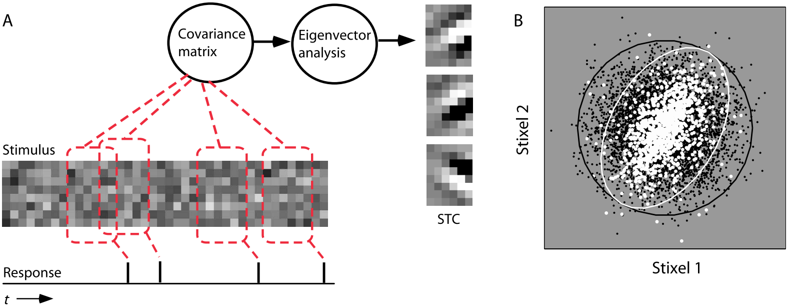


Distribution changes along relevant directions (and, usually, along all linear combinations of relevant directions).

Proxies to measure change in distribution:

- mean: STA (can only reveal a single direction)
- variance: STC
- binned (or kernel) KL divergence: MID “maximally informative directions” (equivalent to ML in LNP model with binned nonlinearity)

STC



Project out STA:

$$\widetilde{S} = S - (S\mathbf{k}_{\text{sta}})\mathbf{k}_{\text{sta}}^{\mathsf{T}}; \quad C_{\text{prior}} = \frac{\widetilde{S}^{\mathsf{T}}\widetilde{S}}{N}; \, C_{\text{spike}} = \frac{\widetilde{S}^{\mathsf{T}}\text{diag}(R)\widetilde{S}}{N_{\text{spike}}}$$

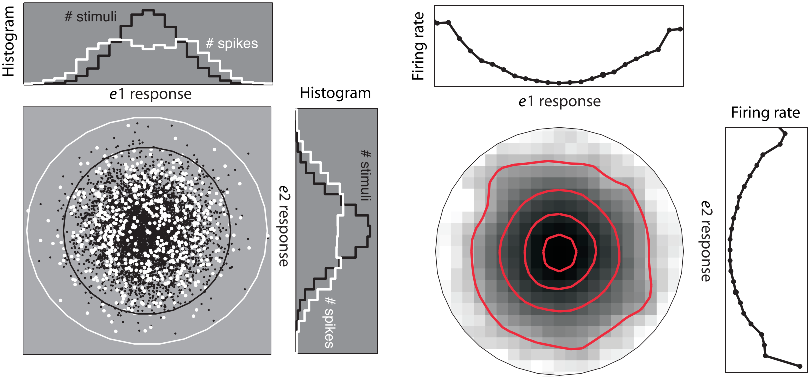
Choose directions with greatest change in variance:

$$\text{k-}\operatorname*{argmax}_{\|\mathbf{v}\|=1} \mathbf{v}^{\mathsf{T}}(C_{\text{prior}} - C_{\text{spike}})\mathbf{v}$$

$\Rightarrow$ find eigenvectors of $(C_{\text{prior}} - C_{\text{spike}})$ with large (absolute) eigvals.

STC

Reconstruct nonlinearity (may assume separability)



Biases

STC (obviously) requires that the nonlinearity alter variance.
If so, subspace is unbiased provided distribution is

- radially (elliptically) symmetric
- AND independent

$\Rightarrow$ Gaussian.

May be possible to correct for non-Gaussian stimulus by transformation, subsampling or weighting (latter two at cost of variance).

More LNP methods

- Non-parametric non-linearities:

  "Maximally informative dimensions" (MID) $\Leftrightarrow$ "non-parametric" maximum likelihood.

  - Intuitively, extends the variance difference idea to arbitrary differences between marginal and spike-conditioned stimulus distributions.

$$\mathbf{k}_{\text{MID}} = \underset{\mathbf{k}}{\operatorname{argmax}} \, \mathbf{KL}[P(\mathbf{k} \cdot \mathbf{x}) \| P(\mathbf{k} \cdot \mathbf{x} | \text{spike})]$$

  - Measuring KL requires binning or smoothing—turns out to be equivalent to fitting a non-parametric nonlinearity by binning or smoothing (Williamson, Sahani, Pillow PLoSCB 2015).
  - Difficult to use for high-dimensional LNP models (but ML viewpoint suggests separable or "cylindrical" basis functions – see Williamson et al.).

- Parametric non-linearities: the "generalised linear model" (GLM).

Generalised linear models

LN models with specified nonlinearities and exponential-family noise.

In general (for monotonic g):

$$y \sim \text{ExpFamily}[\mu(\mathbf{x})]; \qquad g(\mu) = \beta\mathbf{x}$$

For our purposes easier to write

$$y \sim \text{ExpFamily}[f(\beta\mathbf{x})]$$

(Continuous time) point process likelihood with GLM-like dependence of λ on covariates is approached in limit of bins $\to 0$ by either Poisson or Bernoulli GLM.

Mark Berman and T. Rolf Turner (1992) Approximating Point Process Likelihoods with GLIM Journal of the Royal Statistical Society. Series C (Applied Statistics), 41(1):31-38.

Generalised linear models

Poisson distribution $\Rightarrow f = \exp()$ is *canonical* (*natural params* $= \beta\mathbf{x}$).

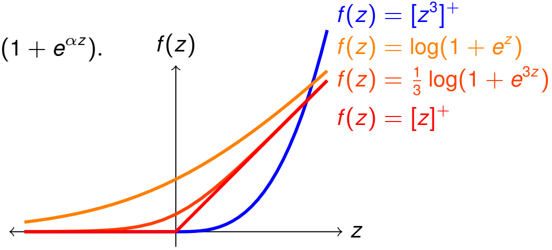
Canonical link functions give concave likelihoods $\Rightarrow$ unique maxima.

Generalises (for Poisson) to any f which is convex and log-concave:

$$\text{log-likelihood} = c - f(\beta\mathbf{x}) + y \log f(\beta\mathbf{x})$$

Includes:

- threshold-linear
- threshold-polynomial
- "soft-threshold" $f(z) = \alpha^{-1} \log(1 + e^{\alpha z})$.



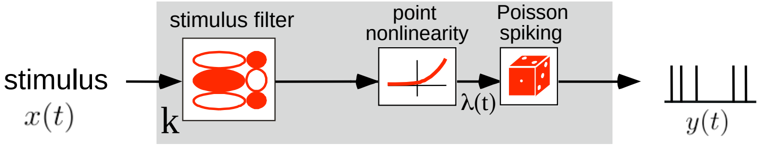
Generalised linear models

ML parameters found by

- gradient ascent
- IRLS

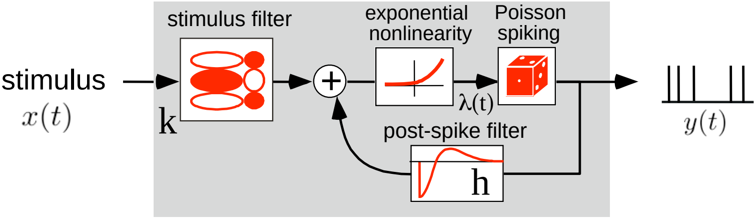
Regularisation by L_2 (quadratic) or L_1 (absolute value – sparse) penalties (MAP with Gaussian/Laplacian priors) preserves concavity.

Linear-Nonlinear-Poisson (GLM)



GLM with history-dependence

(Truccolo et al 04)

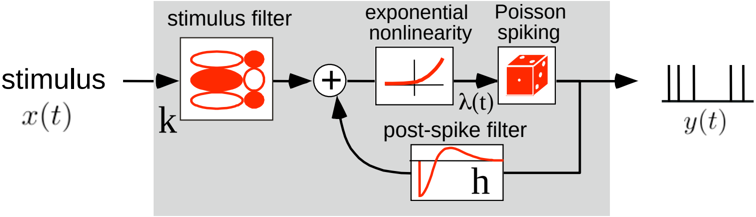


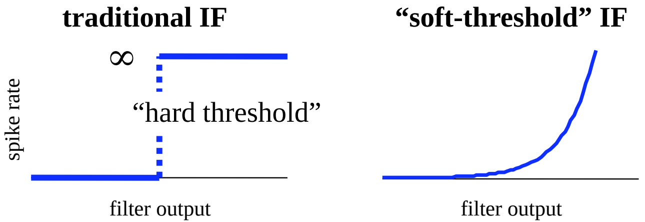
conditional intensity
(spike rate)

$$\lambda(t) = f(k \cdot x(t) \; + \; h \cdot y(t))$$
$$= e^{k \cdot x(t)} \; \cdot \; e^{h \cdot y(t)}$$

- rate is a product of stim- and spike-history dependent terms
- output no longer a Poisson process
- also known as “soft-threshold” Integrate-and-Fire model

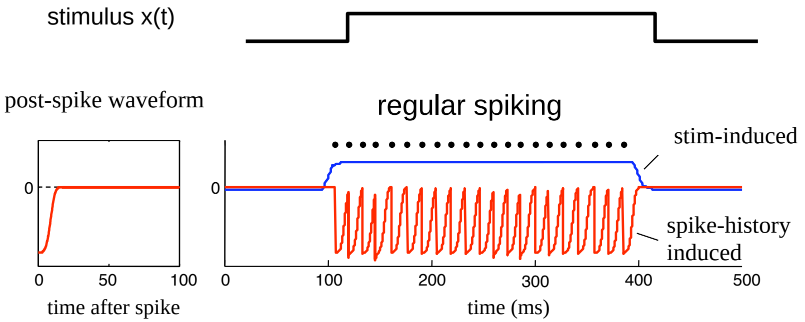
GLM with history-dependence



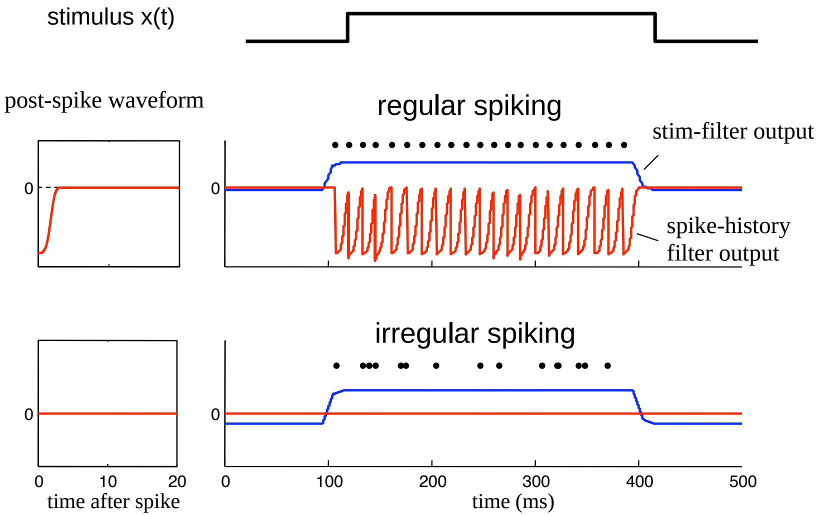


- "soft-threshold" approximation to Integrate-and-Fire model

GLM dynamic behaviors



GLM dynamic behaviors



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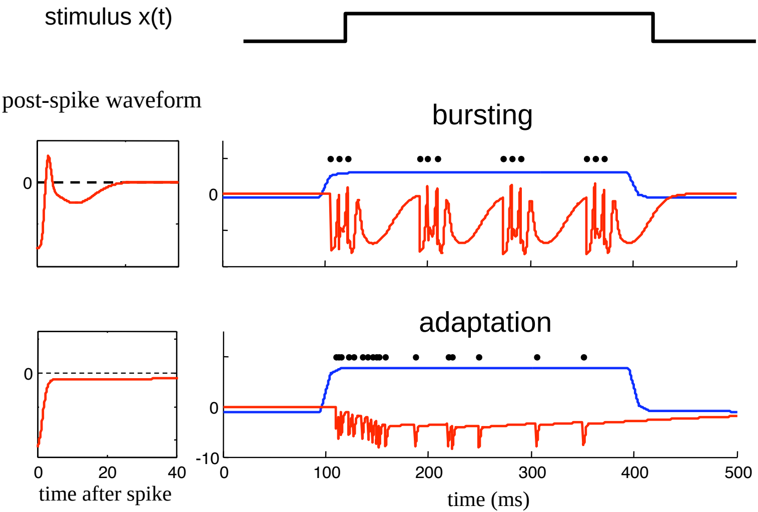
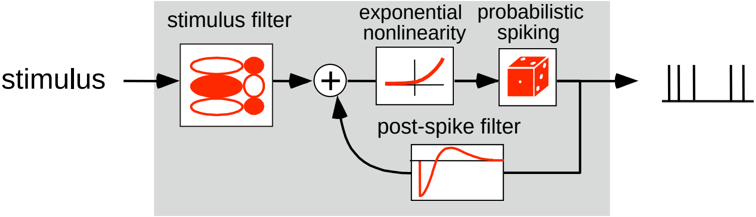
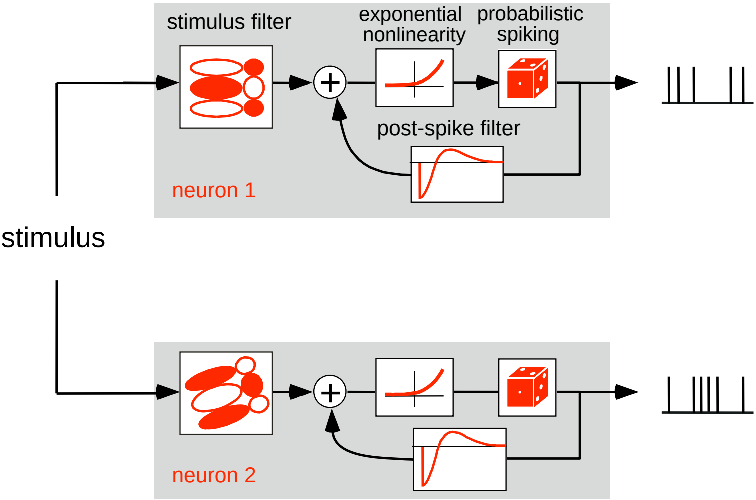


Generalized Linear Model (GLM)



multi-neuron GLM



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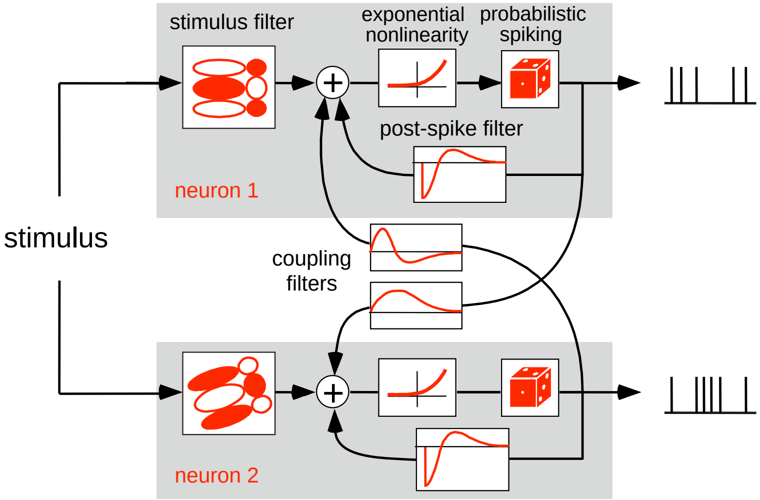
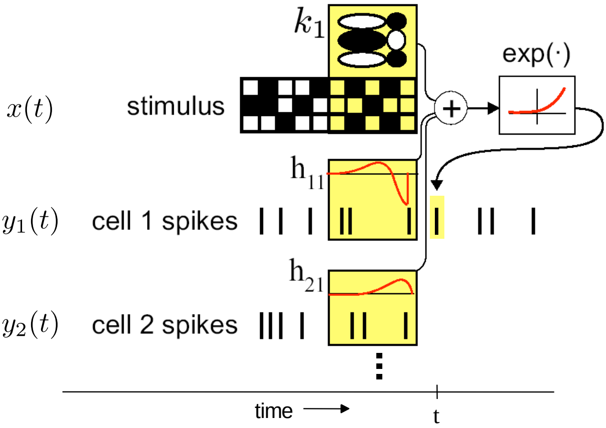


GLM equivalent diagram:



conditional intensity
(spike rate)

$$\lambda_i(t) = \exp(k_i \cdot x(t) \; + \; \textstyle\sum_j h_{ij} \cdot y(t))$$

Non-LN models?

The idea of responses depending on one or a few linear stimulus projections has been dominant, but cannot capture all non-linearities.

- Contrast sensitivity might require normalisation by $\|\mathbf{s}\|$.
- Linear weighting may depend on *units* of stimulus measurement: amplitude? energy? logarithms? thresholds? (NL models – Hammerstein cascades)
- Neurons, particularly in the auditory system are known to be sensitive to combinations of inputs: forward suppression; spectral patterns (Young); time-frequency interactions (Sadogopan and Wang).
- Experiments with realistic stimuli reveal nonlinear sensivity to parts/whole (Bar-Yosef and Nelken).

Many of these questions can be tackled using a multilinear (cartesian tensor) framework.

Input nonlinearities

The basic linear model (for sounds):

$$\underbrace{\widehat{r}(i)}_{\text{predicted rate}} = \sum_{jk} \underbrace{w^{\mathbf{tf}}_{jk}}_{\text{STRF weights}} \underbrace{s(i-j,k)}_{\text{stimulus power}} ,$$

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We can *learn* an optimal representation $g(.)$:

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Define: basis functions $\{g_l\}$ such that $g(s) = \sum_l w^{\mathbf{l}}_l g_l(s)$
and stimulus array $M_{ijkl} = g_l(s(i-j,k))$. Now the model is

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$$\hat{r}(i) = \sum_{jkl} w^{\mathbf{tf}}_{jk} w^{\mathbf{l}}_l M_{ijkl} \quad \text{or} \quad \widehat{\mathbf{r}} = (\mathbf{w}^{\mathbf{tf}} \otimes \mathbf{w}^{\mathbf{l}}) \bullet \mathbf{M}.$$

Multilinear models

Multilinear forms are straightforward to optimise by alternating least squares.

Cost function:

$$\mathcal{E} = \left\| \mathbf{r} - (\mathbf{w}^{\mathsf{tf}} \otimes \mathbf{w}^{\mathsf{l}}) \bullet \mathbf{M} \right\|^2$$

Minimise iteratively, defining *matrices*

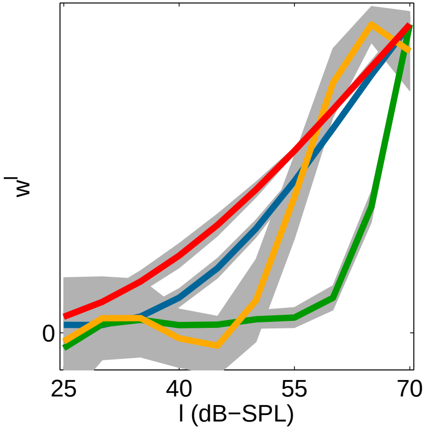
$$\mathbf{B} = \mathbf{w}^{\mathsf{l}} \bullet \mathbf{M} \qquad \text{and} \qquad \mathbf{A} = \mathbf{w}^{\mathsf{tf}} \bullet \mathbf{M}$$

and updating

$$\mathbf{w}^{\mathsf{tf}} = (\mathbf{B}^{\mathsf{T}}\mathbf{B})^{-1}\mathbf{B}^{\mathsf{T}}\mathbf{r} \qquad \text{and} \qquad \mathbf{w}^{\mathsf{l}} = (\mathbf{A}^{\mathsf{T}}\mathbf{A})^{-1}\mathbf{A}^{\mathsf{T}}\mathbf{r}.$$

Each linear regression step can be regularised by evidence optimisation (suboptimal), with uncertainty propagated approximately using *variational* methods.

Some input non-linearities



Variable (combination-dependent) input gain

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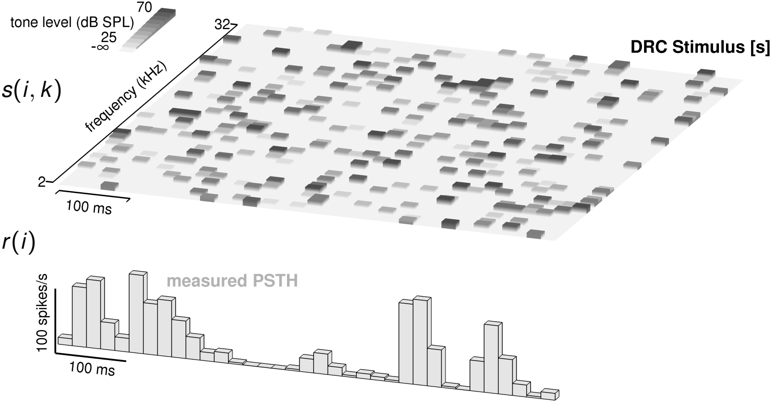
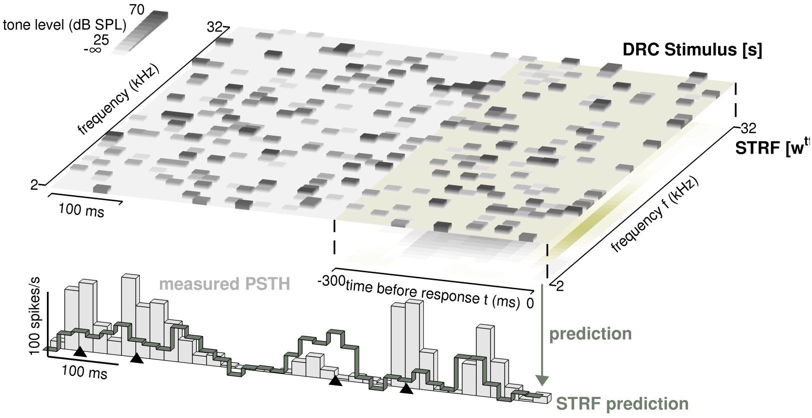
- Sensitivities to different points in sensory space are not independent.
- Rather, the sensitivity at one point depends on other elements of the stimulus that create a *local* sensory context.
- This context adjusts the input gain of the cell from moment to moment, dynamically refining the shape of the weighted receptive field.

Context-sensitive gain



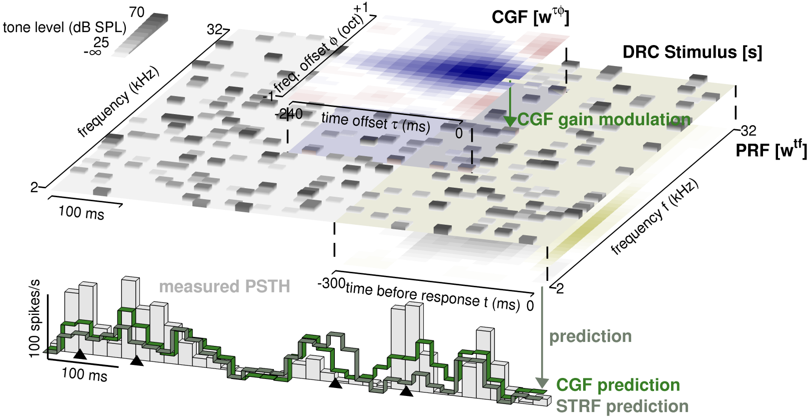
Context-sensitive gain

$$\hat{r}(i) = c + \sum_{j=0}^{J} \sum_{k=1}^{K} w^{tf}_{j+1,k} s(i-j,k)$$



Context-sensitive gain

$$\hat{r}(i) = c + \sum_{j=0}^{J} \sum_{k=1}^{K} w^{tf}_{j+1,k} s(i-j,k) \left(1 + \sum_{m=0}^{M} \sum_{n=-N}^{N} w^{\tau\phi}_{m+1,n+N+1} s(i-j-m,k+n)\right)$$



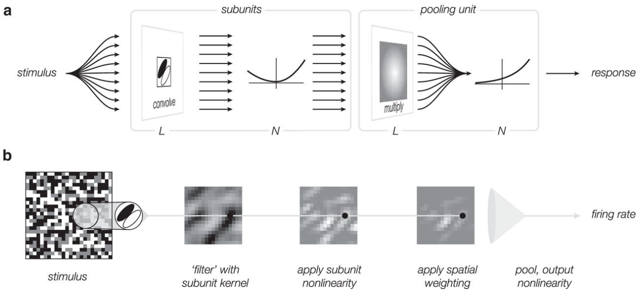
LNLN cascades

- Limited description of 'layered' structure of sensory pathways:

$$\hat{r}(t) = f\left(\sum_{n=1}^{N} w_n g_n\left(\mathbf{k}_n^{\mathsf{T}}\mathbf{s}(t)\right)\right)$$

- $\mathbf{k}_n$ describes the linear filter and g_n the output nonlinearity of each of N input subunits. The g_n are usually fixed half-wave rectifiers.
- Called a generalised nonlinear model (GNM; Butts *et al*. 2007, 2011; Schinkel-Bielefeld *et al*. 2012)
- Or a nonlinear input model (NIM; McFarland *et al*. 2013).
- Parameters estimated by maximum-likelihood using inhomogeneous Poisson noise – often by alternation (following Ahrens et al. 2008).
- Resembles a (perceptron) “neural network”.

Convolutional LNLN



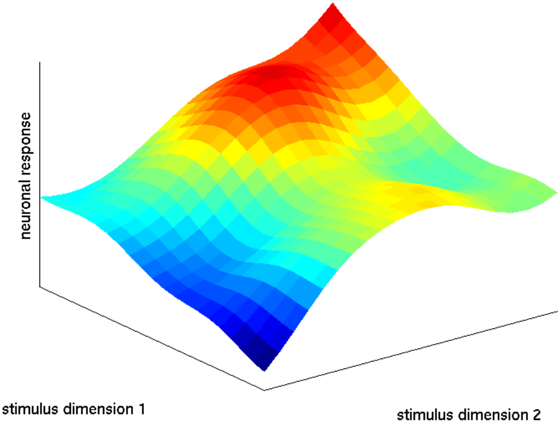
$$\hat{r}(t) = f\left(\sum_{c=1}^{C}\sum_{n=1}^{N} w_{c,n}\sum_{i=1}^{B} b_{c,i}g_i\left(\mathbf{k}_{c,n}^{\mathsf{T}}\mathbf{s}(t)\right)\right)$$

- C "channels" – each uses same kernel $\mathbf{k}_c$ translated to a different location (convolution).
- Input nonlinearities learned using basis expansion and alternation (Ahrens et al. 2008).
- Output nonlinearity f fixed.

Limitations of linear approximations

What are the consequences of nonlinearities in the stimulus-response function for interpretation of structure in linear models like STRFs?

Linear fits to non-linear functions



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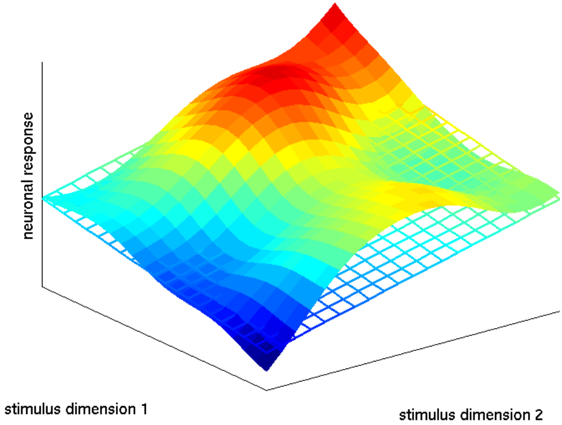
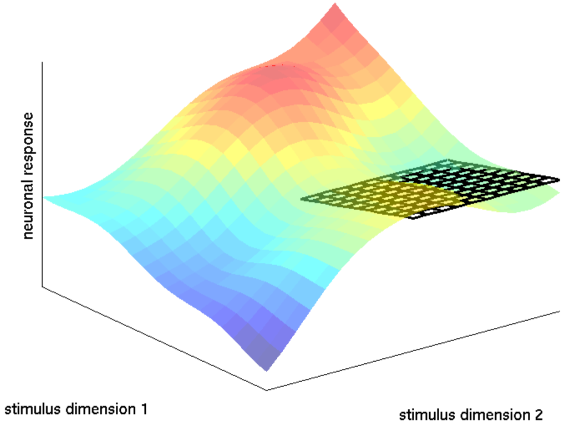


Approximations are stimulus dependent



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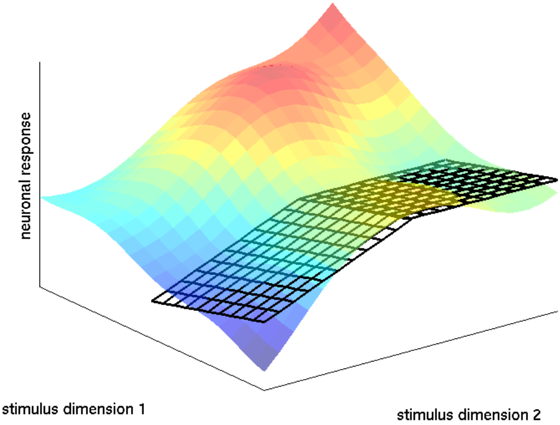

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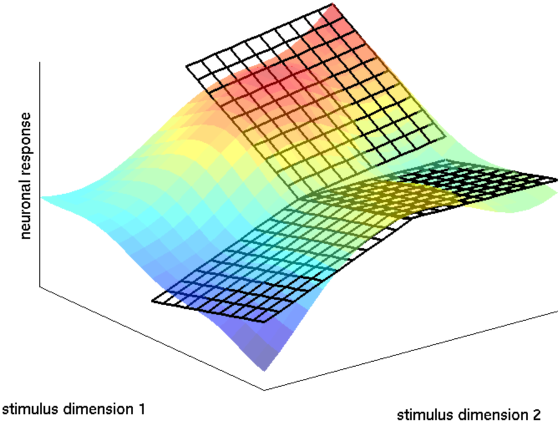

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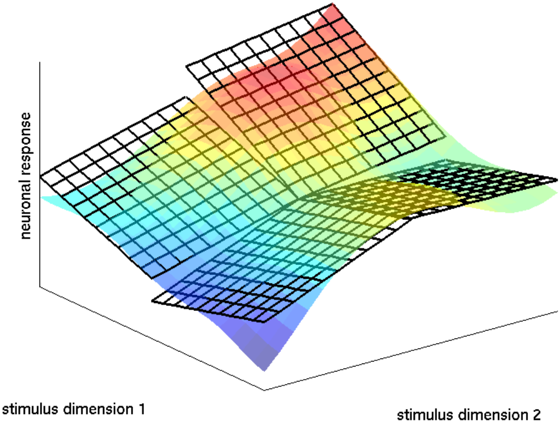

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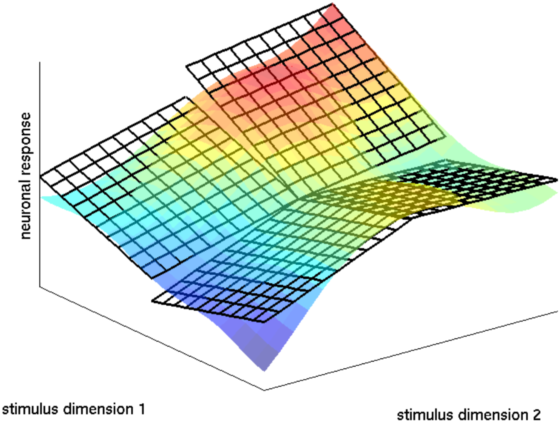


(Stimulus dependence does not always signal response adaptation)

Consequences

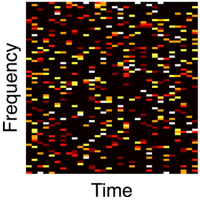
Local fitting can have counterintuitive consequences on the interpretation of a “receptive field”.

“Independently distributed” stimuli

Knowing stimulus power at any set of points in analysis space provides no information about stimulus power at any other point.

DRC:

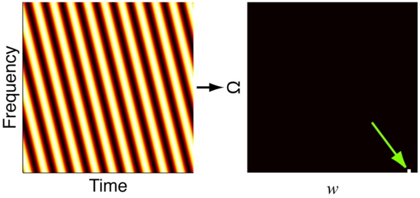
Spectrotemporal Space



Ripple:

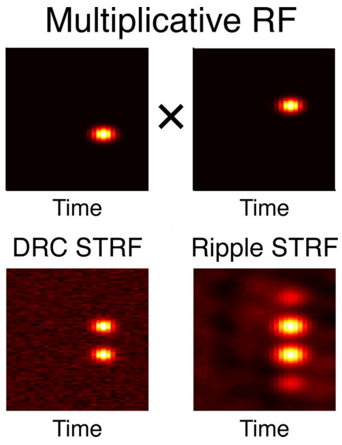
Spectrotemporal Space

Modulation Transfer Space



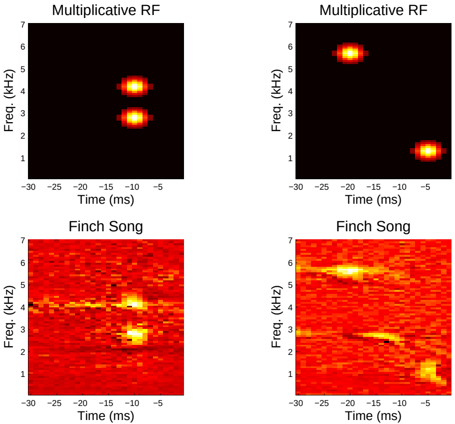
Independence is a property of stimulus *and* analysis space.

Nonlinearity & non-independence distort RF estimates



Stimulus may have higher-order correlations in other analysis spaces — and interaction with nonlinearities can produce misleading “receptive fields.” (Christianson, Sahani and Linden 2008 J Neurosci)

What about natural sounds?



Usually not independent in any space — so STRFs may not be conservative estimates of receptive fields.

Summary

How can we use linear models of neuronal stimulus-response functions most effectively to answer biological questions?

Pay a lot of attention to three key issues:

1. nature of stimulus
   - ethological/physiological relevance?
   - second-order and/or higher-order autocorrelations?
2. choice of stimulus representation
   - appropriate to the biology?
   - appropriate to the question?
3. limitations of linear approximation
   - consequences of likely nonlinearities in stimulus-response function?
   - interaction with higher-order autocorrelation in stimulus?

Linear modelling can be a simple and useful tool for answering specific questions about neural coding of stimuli, but results must be interpreted carefully.